anti-cancer effect. The outcome of allogeneic BMT however, has been negatively impacted by the increased mortality and morbidity due to transplant related toxicities including graft versus host (GVHD) disease. There is an urgent need for a transplant regimen that can combine the benefits of high dose chemotherapy (as used in autologous BMT) with the ones of graft versus tumor (GVT) effects while decreasing the transplant related mortality and morbidity, specifically due to GVHD and related immunosuppressive medications. Establishing a stable and reproducible mixed chimerism status in the host may be an answer to this problem. However most of the current transplant protocols can only result in transient mixed chimerism quickly changing to full donor chimerism or graft rejection. To be able to take advantage of mixed chimerism in a transplant setting, it is essential to have a reliable, and clinically practical transplant regimen that consistently results in stable and predictable mixed chimerism. To achieve this goal, we simultaneously co-transplanted different ratios of allogeneic and syngeneic marrow cells from B6.SJL mice and B6D2F1 mice into B6D2F1 recipients. With this protocol we were able to achieve a stable mixed chimerism lasting more than 6 months. The level of mixed chimerism was very similar to the ratio of the cells given at the time of transplant. We did not observe any GVHD in this animals. We next used the same model in a full mismatch B6.SJL into Balb/c transplant model. No stable mixed chimersm was observed. However, administration of intrperitoneal cyclophosphamide (Cy) 1 day after transplant, resulted in stable mixed chimersim in all the animals. We were able to convert these stable mixed chimersim to either donor or recipient phenotype by administration of allogeneic or autologous spleen cells. Even after DLI, no evidence of overt GVHD was seen. Changes in timing of Cy from day +1 to day 3-4 did not change the outcome of mixed chimerism. Interestingly, we observed some GVT effects in the animals that had mixed chimerism. The simplicity of this transplant model with no need for any in-vitro manipulation of cells and no need for GVHD prophylaxis, plus the reproducibility of the mixed chimerism status, makes this an interesting approach for the treatment of both benign and malignant hematological conditions.

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### NONMYELOABLATIVE AND REDUCED INTENSITY CONDITIONING IN ALLOGENEIC STEM CELL TRANSPLANTATION FOR MYELOFIBROSIS

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**Introduction:** The only potentially curable therapy for myelofibrosis is allogeneic transplantation. Traditionally, myeloablative conditioning regimens have been utilized but have been limited by high regimen related mortality (RRM), poor 5 year overall survival, advanced patient age and comorbidities. For these reasons, NST and RIC have become an attractive transplant modality. We analyzed the results of 16 consecutive patients with MF transplanted using NST and RIC conditioning regimens at our institution.

**Patients and Methods:** Gender: 11 males and 5 females with a median age of 58.5 years (27-68) underwent allogeneic HCT at Mount Sinai Medical Center between 2002 and 2009. The different disease subtypes were: idiopathic MF (8), post-PV MF (1), post-ET MF (1) and MF in transformation to AML (6). Donor sources included bone marrow (6) and peripheral blood stem cells (10). Related donors were used in 6 transplants and unrelated donors in 10. Conditioning regimens used were: NST (6), RIC (9) and MA (1). Patients received CSA/MMF (9) or FK/MTX (7) for immunosuppression.

**Results:** Eight patients are alive with a median follow-up of 329 days (12-1925). Eight patients are dead due to: GVHD (2), infection (5) and MOF (1). Three patients (19%) died from regimen-related mortality prior to day 100 post-transplant. Of these, 2 died from sepsis and 1 from MOF. All 14 evaluable patients achieved 100% donor chimerism. No patients had graft failure or received DLI. Grade II-IV aGVHD developed in 7 patients and grade IV in 2. Limited chronic GVHD developed in 1 patient and extensive in 3.

*Conclusions:* Myeloablative conditioning, comorbid conditions and age are limitations for allogeneic HCT in MF. Our unselected series demonstrates that NST and RIC HCT are feasible, increase the pool of eligible patients, are able to achieve a good donor chimerism and have an acceptable rate of RRM and GVHD.

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### THE ASSOCIATION OF FLUDARABIN, ORAL BUSULFAN AND THYMOGLOBULIN PRIOR TO MATCHED RELATED ALLO-SCT ALLOWS FOR HIGH LONG TERM OUTCOME FOR BOTH PATIENTS WITH MYELOID OR LYMPHOID MALIGNANCIES: LONG TERM ANALYSIS OF A HOMOGENOUS COHORT OF 100 CONSECUTIVE PATIENTS

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We analysed 100 consecutive pts treated in a single centre with a minimal and median follow-up of respectively 28 and 56 mths. Diagnoses: acute leukemia (AL) (39%), myeloid malignancies (HMY) (16%) (AL + HMY = 55%) and lymphoid malignancies (HLY) (45%); all pts were treated with PBSC allo-SCT from a matched-related donor. RIC: oral bu (8 mg/m2), thymoglobuline (2.5 mg/kg) and fludara (150 mg/m2 over 5 days) and. Median age:50 (18-64). Respectively 53, 14 and 33 pts were in CR, progression or stable disease (AL + HMY: 85%, 13%, 2%; HLY: 13%, 16%, 71%, p<.0001). EBMT disease stage evaluation was early (0-1), intermediate (2-3), and high stage (4-6) for respectively 5, 52, 41 pts (AL + HMY: 7%, 73%, 20%; HLY: 2%, 27%, 71%, p<.0001). HCT-CI was 0, 1-2 and >2 in 31, 39 and 23 of the 92 assessable pts (AL + HMY: 36%, 35%, 29%; HLY: 25%, 56%, 19%, p = NS). All but one engrafted. aGVHD and cGVHD CI were 43% (33-54) and 81% (73-89) respectively. cGVHD was associated with low CD34 dose (.0001) and previous Grade ≥ 2 aGVHD (.036). DLI was administered in 16 pts for mixed chimerism or disease progression in respectively 3 and 13 cases. TRM CI at 12 mths and 5 years were 15% (8-22) and 25% (16-34) respectively. TRM was strongly associated with aGVHD (p = .00004) but not with EBMT score nor HCT-CI index. Overall, on the 56 assessable pts, 36 (64%) achieved objective response (no difference between 2 groups). Relapse/progression occurred at a median of 11 mths (1-52) in respectively 21 pts for a CI of 22.4% (11-33.7) and 22.5% (8.7-36.2) respectively in AL + HMY and HLY groups. In a landmark analysis, disease progression was associated with the absence of grade ≥2 aGVHD (p = .0045) and the absence of cGVHD (p = .0035). 5 years OS and PFS probabilities were 63% (51-78) and 61% (49-75) for HMY + LA and 55%(42-72) and 45%(31-64) for HLY. In multivariate analysis, improved PFS was related to CR at transplantation (p = .009) and low CD34 dose (under median) (p = .028). Results suggested a high efficiency of a RIC combining Fludarabin and limited myeloablation (busulfan) and limited thymoglobuline dose in a wide population in term of age, HSCT-CI, EBMT disease stage evaluation for both lymphoid and not lymphoid malignancies. Lower stem cell dose (but not other graft cells) was associated with more cGVHD and improved PFS. This observation deserves further investigation, notably inviting to revisit the impact of GCSF mobilization in RIC context.

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### A SINGLE CENTRE REVIEW INVESTIGATING WHETHER THE TRANSPORT TIMES OF MUD STEM CELLS INFLUENCES ENGRAFTMENT TIMES POST HSCT

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**Aim:** To analyse the impact that travel times and the wait time before infusion has on neutrophil and platelet engraftment and overall mortality in recipients of unrelated donor stem cells.

**Background:** Approximately a third of all Allogeneic stem cell transplants performed now use unrelated donors. Usually donors have stem cells collected at centres distant from the transplant centre. NMDP data indicates that the length of travel time and the wait time before infusion does not affect neutrophil engraftment time. A higher overall mortality was associated with bone marrow grafts which had a combined travel and wait time of ≥ 26 hours.

**Method:** A retrospective chart review was undertaken at Wellington Hospital looking at consecutive MUD transplants between March 2004 and June 2009. Data were collected on the disease, donor location, stem cell source, travel times, wait time at the transplant centre before infusion, neutrophil and platelet engraftment; and early (prior to Day +100) and overall mortality.

**Result:** There were 26 consecutive MUD transplants performed during the study period. A single cord blood transplant was excluded from analysis. 52% donor stem cells had travel times to the transplant centre of ≥ 20 hours. The time between the arrival of stem cells at the transplant centre to infusion into the patient ranged from 1 – 42 hours. Extended travel and wait times did not appear to impact on neutrophil or platelet recovery (median time to neutrophil engraftment = 16 days, platelet engraftment = 20 days) or mortality.

**Conclusion:** The majority of collections for our centre were from Germany. In all cases, combined travel and wait times before infusions were greater than 30 hours. With the caveat of small numbers, there appeared to be no difference in neutrophil and platelet engraftment times or to early or overall mortality. In some cases there were considerable delays between stem cells arriving at the transplant centre and infusion into the patient. Our remote location and the logistics related to flight arrival times and TBI timing make this unavoidable.

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### LOW-DOSE ANTI-T-LYMPHOCYTE GLOBULIN (ATG-FRESIUS) SIGNIFICANTLY REDUCES ACUTE GVHD AND NON-RELAPSE MORTALITY (NRM) AFTER REDUCED-INTENSITY UNRELATED BMT

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**Introduction:** Unrelated HSCT with a reduced-intensity conditioning regimen (RIC) is now widely performed as an alternative to HLA-matched related HSCT. However, the optimal regimen has not yet been well established in Japan, where peripheral blood stem cell transplantation is not yet allowed for unrelated pairs. In this retrospective analysis of unrelated RIC BMT, we evaluated the feasibility of a regimen using a lower dose of rabbit ATG (Fresius) and TBI.

**Patients and Methods:** From January 2000 to May 2009, 108 patients received unrelated BMT with a RIC regimen that included fludarabine or cladribine plus busulfan. Additionally, 30 patients received 4 Gy TBI, 45 received 2 Gy TBI, and 33 received lower doses of ATG (5 mg/kg, n = 20; 10 mg/kg, n = 13). Endpoints included the probability of acute GVHD, engraftment, NRM, overall survival (OS) and progression-free survival (PFS).

**Results:** The probability of grade II-IV acute GVHD was, respectively, 58%, 71%, and 17% in the 4 Gy TBI, 2 Gy TBI and ATG-containing groups (P = 0.0002). The probability of grade III-IV acute GVHD was, respectively, 37%, 9% and 0% in the 4 Gy TBI, 2 Gy TBI and ATG-containing groups (P = 0.0002). There were 7 graft failures in the ATG group (1 primary and 6 secondary), 1 secondary graft failure was observed in the 4 Gy group and 1 primary graft failure was seen in the 2 Gy group. The probability of NRM at 1 year was 48% in the 4 Gy group, 17% in the 2 Gy group and 0% in the ATG group. At 2 years, this was 52% in the 4 Gy group, 23% in the 2 Gy group and 19% in the ATG group (P = 0.003). The probability of death due to relapse/progression at 2 years was 19% in the 4 Gy group, 36% in the 2 Gy group and 32% in the ATG group (P = 0.32). The 2-year OS was 40% in the 4 Gy group, 50% in the 2 Gy group and 60% in the ATG group (P = 0.05). The 2-year PFS was 40% in the 4 Gy group, 50% in the 2 Gy group and 52% in the ATG group (P = 0.21).

**Conclusion:** A lower dose of ATG-Fresius (5-10 mg/kg) significantly reduced the risk of acute GVHD and NRM compared to low-dose TBI after unrelated BMT in a RIC setting, despite an associated higher rate of secondary graft failure. These findings will need to be confirmed in a larger prospective randomized-controlled trial.

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### PROGNOSTIC INDEXES IS NOT PREDICTIVE OF TREATMENT RELATED MORTALITY IN PATIENTS (PTS) OLDER THAN 60 YEARS TREATED WITH REDUCED INTENSITY CONDITIONING AND ALLOGENEIC STEM CELL TRANSPLANTATION (RIC-ALLO)

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**Background:** For many maligant diseases, median age at diagnosis is around the sixth decade of life, precluding myeloablative ALLO. RIC-ALLO is less toxic and has been performed in elderly pts, mainly affected by acute leukemia. Prognostic indexes seem to predict treatment related mortality (TRM) and overall survival (OS).

**Patients and methods:** From 2001 and 2008, 63 pts older than 60 years (median age 63 y, range 60-70) received RIC-ALLO. Diseases were: acute myeloid leukemia 45%, and chronic lymphoproliferative diseases 54%. Disease status at RIC-ALLO was: complete remission 54%, partial remission 16%, and active disease 30%. RIC consisted of fludarabine-based with thymoglobulin 64%, or low-dose TBI-based 36%. Donors were: HLAid sibling 73%, matched unrelated 21%, and cord blood 6%. Three prognostic scores were evaluated.

**Results:** The median follow-up was 22 months. The 2-y OS and PFS were 66.8% (IC95; 55.5-80.4) and 52.4% (IC95:39.5-69.5), respectively. Grade II-IV acute graft versus host disease (aGVHD) and chronic GVHD (cGVHD) incidence were 49% and 43%, respectively. Early infections were fever of unknown origin in 42% of pts, bacterial infection in 6 cases, pneumonia in 8, and viral infections in 14. The early infection-related mortality was null. Late infections were bacterial in 3 cases, pneumonia in 1, viral infections in 6, and candidemia in 1. Seven pts died from late infective complications. Overall, the cause of death was toxicities in 18 pts and disease progression in 6 pts. The 100-d and 1-y TRM were 6% and 24%, respectively.

In univariate analysis, HCT-CI, EBMT score, and PAM score did not influence TRM or OS. Furthermore, age (60-65 vs 66-70) was not related to TRM. Only severe aGVHD was predictive.

**Conclusions:** The aim of this retrospective study was to assess if TRM was excessively high in elderly pts, after ALLO-RIC. A secondary objective was to evaluate if any of the current prognostic indexes could predict TRM and OS in this peculiar population. TRM was acceptable and not different when compared to younger pts as reported in literature. Furthermore, neithe prognostic index nor age help segregating a group of pts with higher TRM limiting their value for treatment decision in this situation.

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### ABSOLUTE NEUTROPHIL COUNT LESS THAN 0.2 × $10^9$/L ON DAY SIXTEEN POST-TRANSPLANT MARKEDLY INCREASES THE RISK OF GRAFT FAILURE

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Following allogeneic hematopoietic stem cell transplantation (HSCT) graft failure is a major complication, which markedly